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Short communication

Analyzing BSE surveillance in low prevalence countries☆

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Abstract

If the prevalence of bovine spongiform encephalopathy (BSE) varies among cohorts within a population, stratified analysis of BSE surveillance data may allow identification of differences in BSE exposure that are important with respect to the design and evaluation of disease prevention and control measures. In low BSE prevalence populations, however, surveillance at levels that meet or exceed international guidelines may provide insufficient statistical power to distinguish prevalence levels among cohorts. Furthermore, over-stratification to account for hypothetical variability in the population may inflate uncertainty in BSE risk estimates.
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1. Introduction

If the prevalence of bovine spongiform encephalopathy (BSE) varies substantially among cohorts within a population, stratified analysis of BSE surveillance data may allow detection of differences in BSE exposure that are important with respect to the design and evaluation of

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disease prevention and control measures. In this regard, the European Food Safety Authority (EFSA) states, ''[t]he ultimate means of determining the effectiveness of [BSE] controls is to estimate the prevalence of infection within birth cohorts before and after the introduction of the interventions'' (EFSA, 2006, p. 29). At low BSE prevalence levels, however, national animal health surveillance at levels exceeding international guidelines provide limited power to statistically distinguish differences in prevalence among cohorts, defined by birth years or otherwise.

Stratified analysis of animal health surveillance data can yield more precise and useful disease prevalence estimates if the stratification variables account for much of the observed variability in the population. However, poor stratification may result in lower precision of the estimated population parameter than simple random sampling when the variance within strata exceeds the variance between strata (Cochran, 1977). Any variance reduction achieved by stratification also must more than compensate for the lost degree of freedom for each stratum. For a fixed sample size, too many strata (overstratification) produces sparseness of data within strata. This may limit statistical power to detect differences among strata and result in strata with zero cases.

Separating uncertainty due to lack of knowledge and variability due to random or systematic heterogeneity also has been promoted as a principle of good risk assessment (Bogen and Spear, 1987; Burmaster and Anderson, 1994; Hoffman and Hammonds, 1994). (See Murray (2002) for an introduction to second-order modeling separating uncertainty and variability in animal health risk analysis.) At least in principle, the prevalence of disease in a population has distinct uncertainty and variability dimensions. Prevalence has a true but unknown value at a specific time and location, and prevalence may vary over time and among subpopulations, regions, etc. However, there may be empirical limitations on the extent to which uncertainty and variability can be disentangled; for example, when variation occurs at a scale smaller than the uncertainty due to measurement error (Baecher, 1999).

The objectives of this paper are to evaluate the statistical power of national BSE surveillance at levels meeting or exceeding international guidelines and to illustrate that overstratification to account for hypothetical variability in the population may inflate uncertainty in BSE risk estimates.

2. Methods

This section begins with a description of the methods used for statistical power analysis. Two scenario analyses were used to evaluate the statistical power of national BSE surveillance at levels meeting or exceeding international guidelines to statistically distinguish differences in prevalence between birth cohorts. A final scenario illustrates that overstratification to account for hypothetical variability of BSE prevalence within a cattle population may inflate uncertainty in the estimated probability of drawing BSE-infected cattle in two-stage sampling when animals are sampled from a randomly selected cohort.

2.1. Statistical power analysis for two independent prevalence samples

The power of a statistical test is the probability of rejecting the null hypothesis (H_0) when it is false. The power depends on the test level of significance (α), the magnitude of effect or difference (δ) under the alternative hypothesis (H_a), sample size (n), and variability in the population (σ^2).

Let:

- p_i = true, unknown disease prevalence in a large population with $i = 1, 2$
- n_i = ith random sample size
- $\alpha = p$ (reject true H_0)
- $\beta = p$ (not reject false H_0)
- power $(1 - \beta) = p$ (reject false H_0)

Under the scenarios considered here, we specify:

- H_0: $p_1 - p_2 = 0$
- H_a: $p_1 - p_2 = \delta$

and assume $n_1 = n_2$ for simplicity.

Assuming a constant probability of disease, the number of cases (c) in a sample (n) from the population varies among random draws according to the binomial distribution:

$$c \sim \text{Binomial}(n, p)$$

where $c = 0, 1, \ldots, n$; n = random sample size and p = disease prevalence.

The prevalence uncertainty distribution is assumed to follow a beta distribution, the conjugate prior to the binomial probability parameter (Rice, 1988):

$$p \sim \text{Beta}\,(a, b)$$

where $\hat{p} = \hat{a}/\hat{a} + \hat{b}$ and $s_p^2 = \hat{a}\hat{b}/(\hat{a} + \hat{b})^2(\hat{a} + \hat{b} + 1)$ are the estimators of p and σ_p^2, respectively.

For $c > 0$, the beta distribution parameters may be estimated using the method of matching moments (Evans et al., 1993):

$$\hat{a} = \hat{p}\left\{\left[\frac{\hat{p}(1 - \hat{p})}{s_p^2}\right] - 1\right\}$$

$$\hat{b} = (1 - \hat{p})\left\{\left[\frac{\hat{p}(1 - \hat{p})}{s_p^2}\right] - 1\right\}$$

where $\hat{p} = c/n$ and $s_p^2 = \hat{p}(1 - \hat{p})/(n - 1)$.

For $c = 0$, however, the matching moments estimates cannot be obtained. (Estimating the beta distribution parameters would involve dividing by zero because the sample variance is zero.) To permit estimation of prevalence for samples with $c = 0$, we estimate the beta distribution parameters assuming a uniform prior on p (Rice, 1988):

$$p_{\text{posterior}} = \text{Beta}(c + a_{\text{prior}},\, n - c + b_{\text{prior}})$$

where $p_{\text{prior}} = \text{Beta}(a_{\text{prior}}, b_{\text{prior}}) = \text{Beta}(1,1) = \text{Uniform}(0,1)$; $\hat{a} = c + 1$; $\hat{b} = n - c + 1$.

The test statistic for comparing two independent prevalence samples is (Rice, 1988):

$$z = \frac{(\hat{p}_1 - \hat{p}_2) - (p_1 - p_2)}{\sigma_{p_1 - p_2}}$$

where $\sigma_{p_1 - p_2} = \sqrt{\sigma_{p_1}^2 + \sigma_{p_2}^2}$.

Under H_0: $p_1 - p_2 = 0$. Under H_a: $p_1 - p_2 = \delta$. As a consequence of the asymmetric sampling distribution of the z statistic under the alternative hypothesis in low prevalence applications, conventional estimation methods overstate the sample size needed to detect a difference between two populations with a specified significance level and power (Williams et al., 2007). Here, however, we make the simplifying assumption that the standard normal ($z \sim N(0,1)$) approximation is sufficient to assess the power of a test to distinguish prevalence levels between cohorts in low BSE prevalence countries. The impact of this standard simplifying assumption is to underestimate the statistical power for a fixed sample size, the degree of underestimation depending on p_1 and δ.

By convention, we set $\alpha = 0.05$ for a two-tailed significance test. (A two-tailed test considers that prevalence may increase or decrease relative to a baseline.) Therefore, the power of the test under H_a: $p_1 - p_2 = \delta$ is approximated by (Rice, 1988):

$$(1 - \beta) \approx 1 - \Phi\left[1.96 - \frac{\delta}{\sigma_{p_1 - p_2}}\right] + \Phi\left[-1.96 - \frac{\delta}{\sigma_{p_1 - p_2}}\right]$$

where Φ = standard normal cumulative distribution function.

For fixed n, the statistical power expression can be evaluated as a function of δ. Other things being equal, the greater the difference in prevalence between two populations, the greater the power of the test.

2.2. Scenario 1—OIE guidelines for BSE surveillance

Scenario 1 is intended to illustrate the statistical power of national BSE surveillance satisfying, but not exceeding, international guidelines. The approach used under the World Organization for Animal Health (OIE) Guidelines for BSE Surveillance assigns 'point values' to each sample that reflect the likelihood of detecting infected cattle within broadly defined surveillance strata (OIE, 2006, Appendix 3.8.4).

Alternatively, countries may use a more refined statistical model, such as the European Union (EU) BSurvE model (Wilesmith et al., 2004, 2005; Prattley et al., 2007) to estimate the random sample size equivalent of targeted BSE surveillance data. Under BSurvE, one BSE surveillance point is estimated to be equivalent to an animal randomly selected for testing from the national herd using a perfect diagnostic test. BSurvE uses a country's epidemiologic information to predict parameters such as incubation period of BSE, probable length of an infected animal's life, and the dynamics of disease expression in infected animals. Because this information is unavailable in countries that have observed few or no BSE cases, default values based on European data provide useful surrogates. BSurvE combines this epidemiologic information with country-specific demographic information about a national herd (size and age distribution) and national BSE surveillance data to obtain a set of point values for samples taken from cattle of different age and surveillance streams—healthy slaughter, fallen stock, casualty slaughter, or clinical suspect. The points represented by an animal tested for BSE are based on the relative likelihood that the disease would be detected in an animal leaving the herd at a particular age and by a particular surveillance stream.

The OIE Guidelines for BSE Surveillance (Type A) call for countries to accumulate 300,000 BSE surveillance points over seven consecutive years to achieve a nominal design prevalence of one case per 100,000 in the adult cattle population at a confidence level of 95% (OIE, 2006, Appendix 3.8.4). Assuming the binomial distribution with zero cases observed in a random sample:

$$1 - (1 - p_d)^n = \mathrm{CL}$$

where p_d (design prevalence) = 1×10^{-5}; n (random sample size) = 300,000; CL (confidence level) = 0.95.

Thus, the OIE BSE surveillance points target is based on an apparent design prevalence that equates to true disease prevalence under the assumption of perfect test sensitivity and specificity. BSurvE input parameters allow the user to adjust the estimated random sample size equivalent to account for less than perfect test sensitivity. Under the default setting, BSurvE assumes that test sensitivity is 100% for clinical animals, 40% within 1 year prior to the onset of clinical BSE symptoms, and zero if sampling occurs more than 1 year prior to clinical onset.

To simplify the scenario analysis, assume that over a period of seven consecutive years, a national BSE surveillance program accumulates the equivalent of $n = 42{,}857$ random samples per birth year cohort, adjusted to account for an imperfect test, to estimate true BSE prevalence. Note that the case of zero infected animals in a cohort sample presents a threshold for prevalence, which we specify as p_0. By convention, we solve for the minimum difference in prevalence ($\delta = p_1 - p_0$) under the alternative hypothesis such that the power of the test ($1 - \beta$) $\geq 80\%$ (i.e., $\beta < 0.2$).

2.3. Scenario 2—diminished power in low prevalence populations

Scenario 2 considers sampling at levels far exceeding the OIE guidelines for BSE surveillance and illustrates the diminished statistical power of sampling to detect substantial differences in prevalence in low prevalence populations. Consider two hypothetical countries that have accumulated 1 million BSE surveillance points (random sample equivalents) for each of two birth cohorts. Under this scenario, the birth cohorts may represent multiple birth years, such as animals born before and after introduction of a ruminant-to-ruminant feed ban. The two countries differ, however, with respect to their initial prevalence. Assume that the initial prevalence in "Country A" is 1 per 10,000, while that in "Country B" is 1 per 100,000. Under this scenario, we calculate the power of the sampling in each hypothetical country to detect a 50% decline in BSE prevalence between cohort 1 and cohort 2. Because this scenario does not require estimation of prevalence for samples with zero cases, we simplify the analysis by using the maximum likelihood estimate of prevalence ($p = c/n$).

2.4. Scenario 3—overstratification inflates uncertainty in BSE risk estimates

Spatial and temporal overdispersion (clustering) of a hazardous agent may result in "hot spots" and/or "hot moments" of risk greater than predicted under the assumption of random variation about a constant mean level. FAO/WHO (2003, p. 23) recommends that clustering of pathogens in food and water "must be taken into account when estimating health risks." In an animal health risk context, for example, feedlot cattle are likely to be processed as a group, or producers may contract with suppliers from a particular region. Animal health risk estimates that account for this non-random mixing of animals may be impacted by extra-binomial variability due to heterogeneity in the prevalence of infection among subpopulations. However, a cohort of animals may be defined by any number of common characteristics, and cattle cohorts may or may not represent distinct subpopulations with respect to BSE prevalence.

Scenario 3 illustrates how overstratification to account for hypothetical variability of BSE prevalence within a cattle population may inflate uncertainty in the estimated probability of drawing BSE-infected cattle in two-stage sampling when animals are sampled from a randomly selected cohort. Assume that a large cattle population consists of 12 cohorts (defined by 4

geographic regions and 3 market classes) of equal size. BSE prevalence estimates are based on 300,000 random sample equivalents evenly distributed among the 12 cohorts:

- $n = \sum_{i=1}^{k} n_i = 300,000$, with $k = 12$ and $n_i = 25{,}000$ for all i
- $w_i =$ proportion of animals in the i^{th} cohort $= 1/k = 1/12$

Assume a total of 60 cases are observed:

$$c = \sum c_i = 60$$

In setting up Scenario 3, the number of cases per cohort (c_i) was obtained by drawing random values from a binomial distribution with a fixed prevalence of 2×10^{-4}:

$$c_i \sim \text{Binomial}(25,000,\ 2 \times 10^{-4})$$

One simulated sampling outcome of cases among cohorts, shown in Table 1, results in cohort prevalence estimates that vary by an order of magnitude (from 4×10^{-5} to 4×10^{-4}). Given this range, intuition might suggest heterogeneity in prevalence among cohorts. However, any apparent differences among cohorts are strictly due to random sampling variability.

In a real world case, however, we would be uncertain, based on the data in Table 1, whether prevalence varies among cohorts. A likelihood ratio test is used to evaluate whether the simulated data indicate heterogeneity in BSE prevalence among cohorts. Under H_0, the cohorts represent a single population with a common BSE prevalence (p) with maximum likelihood estimate:

$$\hat{p} = \frac{\sum c_i}{\sum n_i} = 2 \times 10^{-4}$$

Under H_a, the cohorts represent subpopulations with different BSE prevalence values (p_i) with maximum likelihood estimates shown in Table 1:

$$\hat{p}_i = \frac{c_i}{n_i} = 2.4 \times 10^{-4}, 8.0 \times 10^{-5}, \ldots, 2.4 \times 10^{-4}$$

Table 1
Surveillance data under Scenario 3

Cohort	Sample size (n)	Cases (c)	Prevalence (p)
1	25,000	6	2.4×10^{-4}
2	25,000	2	8.0×10^{-5}
3	25,000	1	4.0×10^{-5}
4	25,000	10	4.0×10^{-4}
5	25,000	7	2.8×10^{-4}
6	25,000	4	1.6×10^{-4}
7	25,000	4	1.6×10^{-4}
8	25,000	5	2.0×10^{-4}
9	25,000	3	1.2×10^{-4}
10	25,000	5	2.0×10^{-4}
11	25,000	7	2.8×10^{-4}
12	25,000	6	2.4×10^{-4}
Total	300,000	60	2.0×10^{-4}

The likelihood ratio is given by

$$L = \frac{\prod_i \text{Binomial}(\hat{p}|c_i, n_i)}{\prod_i \text{Binomial}(\hat{p}_i|c_i, n_i)}$$

The likelihood ratio test statistic is $-2 \log L$. With $k = 12$ strata (cohorts) and $k - 1$ degrees of freedom (d.f.), the distribution of $-2 \log L$ under the null hypothesis is chi-square with d.f. $= 11\left(\chi^2_{11}\right)$ (Rice, 1988).

If we fail to reject the null hypothesis, we would correctly assume that the cohorts have the same prevalence, estimated by $\hat{p}$. However, we can evaluate the effect on the risk estimate of accounting for hypothetical variability by assuming that the cohorts have different prevalence values, estimated by $\hat{p}_i$.

Under the assumption of heterogeneous prevalence, we simulate the probability of drawing a number of BSE-infected animals (c_g) when a group of 25,000 cattle is sampled from a randomly selected cohort:

$$c_g \sim \text{Binomial}(25,000,\ p_c)$$

where p_c is the mixing distribution in which equal weights $(w_1, \ldots, w_{12} = 1/12)$ are given to the cohort prevalence estimates $(\hat{p}_1, \ldots, \hat{p}_{12})$, and $\hat{p}_i \sim \text{Beta}(\hat{a}_i, \hat{b}_i)$.

Under the assumption of homogeneous prevalence:

$$c_g \sim \text{Binomial}(25,000,\ \hat{p})$$

where $\hat{p} \sim \text{Beta}(\hat{a}, \hat{b})$, with $\hat{a}$ and $\hat{b}$ estimated based on $c = \Sigma c_i$ and $n = \Sigma n_i$ using the method of matching moments.

Because $c_i > 0$ for all cohorts, there is no need to specify a prior on prevalence. Therefore, $\text{Beta}(\hat{a}_i, \hat{b}_i)$ and $\text{Beta}(\hat{a}, \hat{b})$ were estimated using the method of matching moments described above. Monte Carlo methods were used to estimate the probability distribution of the number of BSE-infected animals in a group of 25,000 cattle under both assumptions (heterogeneous and homogeneous prevalence). A one-dimensional Monte Carlo simulation was performed that treats random sampling variability as an *a priori* uncertainty distribution for a sample drawn from the population. Monte Carlo simulation was performed (50,000 iterations) using Palisades© @Risk™ (Ver. 4.5), an add-on to Microsoft© Excel™ (2003).

3. Results

3.1. Scenario 1—OIE guidelines for BSE surveillance

Under this hypothetical scenario designed to illustrate the power of BSE surveillance at levels that meet, but do not exceed, international guidelines, the case of zero infected animals in a cohort sample presents a threshold for prevalence (p_0). Using a uniform prior, we estimate the expected value and variance of p_0 to be 2.33×10^{-5} and 5.44×10^{-10}, respectively. Fig. 1 shows the relationship between statistical power to reject the null hypothesis (H_0: $p_0 - p_1 = 0$) and alternative prevalence values (p_1). The statistical power of BSE surveillance under Scenario 1 exceeds 80% for $p_1 \geq 2.45 \times 10^{-4}$ (245 per million).

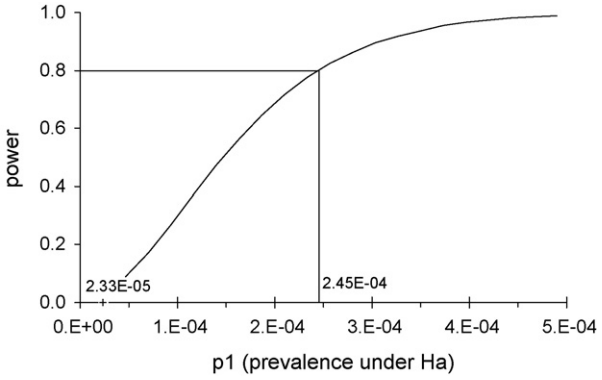

Fig. 1. Relationship between statistical power and alternative prevalence values under Scenario 1.

3.2. Scenario 2—diminished power in low prevalence populations

Under this scenario, sampling levels far exceed the OIE Guidelines for BSE Surveillance. At a 5% significance level, the power of the surveillance in Country A (initial prevalence of 1 per 10,000) to detect a 50% decline in BSE prevalence between two cohorts is 98%. In comparison, the corresponding power of the surveillance in Country B (initial prevalence of 1 per 100,000) to detect a 50% decline in BSE prevalence between cohorts is 25%. In Country B, an order of magnitude decline (from 10^{-5} to 10^{-6}) would be required for the power of the surveillance under Scenario 2 to approach the conventional minimum statistical power criterion of 80%. Of course, the diminished power of the surveillance to detect changes in low prevalence populations also applies to increases in prevalence. At a 5% significance level, the surveillance in Country A provides a power of 80% to detect an increase a 44% increase in prevalence (from 1×10^{-4} to 1.44×10^{-4}). In Country B, a prevalence increase of 170% (from 1×10^{-5} to 2.7×10^{-5}) would be required.

3.3. Scenario 3—overstratification inflates uncertainty in BSE risk estimates

As expected under Scenario 3, the likelihood ratio test correctly supports the null hypothesis that the population is homogeneous with respect to disease prevalence (i.e., with -2 log likelihood = 14.14 and $\chi^2_{0.05,11} = 19.68$, we fail to reject H_0 at the 5% significance level). As a result, there is no basis for incorporating a clustering effect on risk estimates. Assuming either homogeneous or heterogeneous prevalence, the expected number of BSE-infected animals in a group of 25,000 cattle is 5. However, under the assumption of homogeneous prevalence, the estimated 95th percentile of the cumulative probability distribution is 9, while the corresponding estimate is 12 under the assumption of heterogeneous prevalence (Fig. 2).

Scenario 3 also provides an example of the potential problems associated with analyzing post hoc grouping of cohorts. If we collapse cohorts 1–3 into a stratum defined by all market classes in one region with $\hat{p}_1 = 1.2 \times 10^{-4}$ and cohorts 4–12 into a second stratum corresponding to the remaining three regions with $\hat{p}_2 = 2.3 \times 10^{-4}$, a conventional two-tailed z-test would reject H_0: $p_1 - p_2 = 0$ at a significance level of 0.037. (In comparison, the likelihood ratio test would reject the null hypothesis of homogeneous prevalence at a significance level of 0.059.) As above, the expected number of BSE-infected animals in a sample of 25,000 cattle is 5, but under the

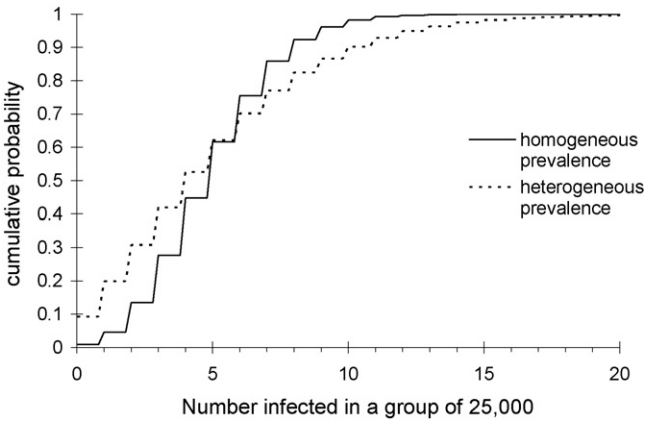

Fig. 2. Cumulative probability distribution of the number of BSE-infected animals in a group of 25,000 cattle under Scenario 3.

assumption of heterogeneous prevalence, the estimated 95th percentile of the cumulative probability distribution is 10. (As above, the estimated 95th percentile under the assumption of homogeneous prevalence is 9.)

4. Discussion and conclusion

In sum, the scenario analyses have demonstrated that BSE surveillance at levels that meet or exceed international guidelines may provide insufficient statistical power to distinguish prevalence levels among cohorts in low BSE prevalence populations. In addition, over-stratification to account for hypothetical variability in the population may inflate uncertainty in BSE risk estimates. The scenario results simply reinforce intuition arising from a basic understanding of statistical sampling and rare events. Nevertheless, formalizing this understanding is important in light of the consequences of BSE for public health and trade.

An important implication of the diminished statistical power of sampling in low prevalence populations is that BSE surveillance data alone are unlikely to provide a purely statistical basis for making a determination about the date when a ruminant-to-ruminant feed ban becomes effective in a low BSE prevalence country. For example, despite the presence of a large-scale active BSE surveillance program, application of the BSurvE model to Netherlands BSE surveillance data suggests the difficulty of drawing clear distinctions in prevalence among birth year cohorts (Heres et al., 2005, Appendix Table 4.1). As a point of reference, according to the OIE, the Netherlands had an annual incidence of reported BSE cases ranging from 0.8 to 13.2 per million adult cattle during 1997–2005 (http://www.oie.int/eng/info/en_esbincidence.htm). Among the original 15 EU member states, only Finland, Greece, and Sweden had a lower incidence of BSE cases (0 per million) reported to OIE in 2005 than the Netherlands (0.8 per million).

The example of inflated uncertainty in BSE risk estimates arising from overstratification also provides an important cautionary tale. Without good prior information about the population, selecting stratification variables can be speculative. While birth year cohorts are intuitively appealing, there is no definitive answer to how narrowly or broadly a cohort should be defined. For example, a cohort could be defined by birth date, market class, geographic location, feed

source, and other attributes. For a given level of surveillance, as cohorts are more narrowly defined, the sample size per cohort decreases and uncertainty about cohort prevalence increases. Without the discipline of empirical evidence and analysis to support the conclusion that stratification is warranted, there is no limit to hypothetical variability. On the other hand, BSE surveillance in low prevalence countries is unlikely to provide sufficient statistical power to detect real heterogeneity in prevalence among cohorts. This conundrum reflects the difficulty in practice of attempting to completely separate uncertainty (a lack of knowledge) and variability (heterogeneity) in risk assessment.

References

Baecher, G.B., 1999. Inaccuracies associated with estimating random measurement errors. J. Geotech. Geoenviron. Eng. 125, 79–80.

Bogen, K.T., Spear, R.C., 1987. Integrating uncertainty and interindividual variability in environmental risk assessment. Risk Anal. 7, 427–436.

Burmaster, D.E., Anderson, P.D., 1994. Principles of good practice for the use of Monte Carlo techniques in human health and ecological risk assessments. Risk Anal. 14, 477–481.

Cochran, W.G., 1977. Sampling Techniques, 3rd ed. John Wiley & Sons, New York.

EFSA (European Food Safety Authority), 2006. Draft Opinion of the Scientific Panel on Biological Hazards on the Revision of the Geographical BSE Risk Assessment (GBR) Methodology. EFSA, Brussels.

Evans, M., Hastings, N., Peacock, B., 1993. Statistical Distributions, 2nd ed. John Wiley & Sons, Inc., NY.

FAO/WHO (Food Agriculture Organization of the United Nations/World Health Organization), 2003. Hazard Characterization for Pathogens in Food and Water: Guidelines. FAO/WHO, Rome.

Heres, L., Elbers, I., Schreuder, B., van Ziderveld, F., 2005. BSE in Nederland. CIDC-Lelystad, Wageningen. , http://www.cidc-lelystad.wur.nl/NR/rdonlyres/C965BF6E-16C1-446A-B3D2-64DB72616494/11387/BSEinNederland.pdf.

Hoffman, F.O., Hammonds, J.S., 1994. Propagation of uncertainty in risk assessments: the need to distinguish between uncertainty due to lack of knowledge and uncertainty due to variability. Risk Anal. 14, 707–712.

Murray, N., 2002. Import Risk Analysis: Animals and Animal Products. MAF Biosecurity, Wellington, New Zealand.

OIE (Office International des Epizooties), 2006. Terrestrial Animal Health Code (2006). OIE, Paris.

Prattley, D., Morris, R., Cannon, R., Wilsemith, J., Stevenson, M., 2007. A model (BSurvE) for evaluating national surveillance programs for bovine spongiform encephalopathy. Prev. Vet. Med. 81, 225–235.

Rice, J.A., 1988. Mathematical Statistics and Data Analysis. Wadsworth & Brooks/Cole, Pacific Grove, CA.

Wilesmith, J., Morris, R., Stevenson, M., Cannon, R., Prattley, D., Benard, H., 2004. Development of a Method for Evaluation of National Surveillance Data and Optimization of National Surveillance Strategies for Bovine Spongiform Encephalopathy, A Project Conducted by the European Union TSE Community Reference Laboratory. Weybridge, United Kingdom, Veterinary Laboratories Agency.

Wilesmith, J., Morris, R., Stevenson, M., Cannon, R., Prattley, D., Benard, H., 2005. BSurvE: a model for evaluation of national BSE prevalence and surveillance. In: User Instructions For the BSurvE Model, Veterinary Laboratories Agency, Weybridge, United Kingdom.

Williams, M., Ebel, E., Wagener, B., 2007. Monte Carlo based sample sizes for determining power in low-prevalence applications. Prev. Vet. Med. 82, 151–158.